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THE ACTION OF BRIEF POLARIZING CURRENTS ON THE CEREBRAL CORTEX OF THE RAT (1) DURING CURRENT FLOW AND (2) IN THE PRODUCTION OF LONG-LASTING AFTER-EFFECTS

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During the course of work on the effects of polarizing currents on the electrical activity of the rat cerebral cortex, we found that prolonged changes in the level of cortical activity could be produced by relatively brief periods of polarizing. This paper describes the after-action of trans-cortical polarizing current upon the activity evoked by stimulating the forepaw and upon spontaneous firing in cortical neurones.

METHODS

Experimental Animals

About 200 albino rats of 200–250 g body weight were used. Each rat was anaesthetized with intraperitoneal urethane (36 % solution, 0·5 c.c./100 g) and fixed in a rigid head-holder. The cortical surface was exposed by making a trephine hole 4 mm dia. and attaching a polyethylene cup to the skull as described by Bindman, Lippold & Redfearn (1962*a*) or by drilling 500 μ dia. holes with an electric drill. Body temperature was maintained within 0·2° C of a given temperature, usually 35° C, with a 12 V heater driven by an OC 35 transistor, controlled by a thermistor in the rectum.

Stimulation and polarization

For evoked potential studies, stimuli were delivered at 2 sec intervals to the skin of the forepaw by means of two fine stainless steel needles inserted beneath the skin. The pulse generator gave 200 μsec square waves which were isolated from earth and fed to the preparation by a 1:1 transformer.

The polarizing circuit consisted of a battery across which was connected a potentiometer. A series swamping resistance of 10 MΩ was used in order to minimize any effects due to variation in resistance of the electrodes or the preparation. A galvanometer having a deflexion of 4 cm/μA enabled the current flowing in the circuit to be measured.

Electrodes

Glass micro-pipettes, usually filled with 10 % NaCl solution (and some filled with 1·8 % NaCl and some with 11 % KCl), were connected to the pre-amplifier by Ag-AgCl wire. Tip diameters were from 0·5 to 20 μ according to requirements. In some experiments non-polarizable wick electrodes or agar gel ones were used for polarizing.

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Electrical recording

The signal from the recording electrodes, one either on the pia or in the cortical grey matter and the second at an indifferent point, was led via a short screened cable to a cathode follower stage. This fed a d.c. channel for recording the wave-form of the evoked potential and an a.c. channel for amplifying the action potential spikes of individual neurones.

Both channels were recorded on either stationary or moving film during certain parts of each experiment.

Measurement

Evoked potentials. In early experiments the peak-to-peak amplitude of each evoked potential was measured using a millimetre scale and plotted by hand. Later a photographic technique was adopted. This consisted of a delayed pulse originated by the stimulus generator, which brightened the beam on the oscilloscope at the time when the negative wave of the evoked potential reached its maximum amplitude. The latency of the negative wave varies less when it is recorded from the depth of minimum latency (300–500 μ below the pia) and most of the experiments were therefore done with the micro-pipette tip at this depth. The delay and duration of the brightening pulse were adjusted at the beginning of each experiment to ensure that the peak of every evoked potential was included in the brightened strip. Use of a stationary spot on the screen and slow moving bromide paper resulted in a trace of dots or dashes, each representing the peak amplitude of the evoked potential. It was also possible to measure the amplitude of background activity by adjusting the spot brilliance to give a faint continuous trace; recorded below this were the evoked potential dots.

Unitary spikes. A sample usually of 4–6 active units was recorded extracellularly. The output of the pre-amplifier was fed through a limiter and a pulse-shaping circuit to dekatron counters. In the initial experiments the counters were controlled by an electronic gate which enabled spike counts to be made during 10 sec periods. Later, a frequency discriminator circuit was used, which gave a voltage output proportional to the frequency of the input pulses. This voltage was sampled at 2 sec intervals by means of the beam brightening circuit described above, and gave a similar trace of dots whose distance from the base line indicated firing frequency. It could be used either in the presence or absence of stimulation of the fore-paw.

In some experiments the spikes and evoked potentials were recorded on magnetic tape, before, during and after polarization for subsequent comparison and analysis.

Histological control of tip location. The procedure adopted to locate the precise position of the micro-pipette tip (e.g. in experiments involving thalamic nuclei) have already been described in detail (Bindman, Lippold & Redfearn, 1964).

Controls and precautions necessary to obtain prolonged effects

Depth of anaesthesia. It was found necessary to adjust the depth of anaesthesia within precise limits. If it was too deep there were few units firing in the grey matter and it appeared to be a matter of chance whether these were affected by the current flow. If the anaesthesia was too light it was easy to produce quite large effects but movements of the animal were liable at any stage to terminate the experiment. As a general guide we aimed at a level of anaesthesia where the burst activity of neurone groups occupied about $\frac{1}{2}$ to $\frac{1}{4}$ of the time; during the rest of the time the base line was flat.

Movement of the micro-electrode. Precautions were taken to prevent extraneous vibration from affecting the relative position of the tip and cortical substance.

Routinely, 1$\frac{1}{2}$–2 hr was allowed from the time of insertion of the electrode until the experiment was begun. This enabled any injury potentials to die away and ensured that any slow movements between cortical tissue and the micro-electrode would have taken place before recording began.

Injury potentials. It was clear that injury discharges were produced in the cortex by the presence of the micro-electrode. While these usually declined in frequency with time, and

were no longer present after ½ hr, sometimes they persisted for more than the 2 hr period. In these circumstances, although the injury potentials were affected by polarizing current, the experiment was rejected. Injury potentials were easily recognized by their regularity of discharge, the fact that they were produced by movement of the electrode tip and because their frequency differed from other potentials occurring in the vicinity. Stopp & Whitfield (1963) have shown that changes in firing rate of single units in the trapezoid body of the cat occurred when a micro-electrode was inserted into the corresponding cochlear nucleus. These changes averaged about 20 % of the control value, being either an increase or decrease in rate.

Temperature. Provided body temperature was kept at 35° C and the anaesthesia was maintained at a constant level, the firing rate was about the same (after allowing time for the cortex to 'settle-down') in any part of the cerebral cortex below 500 μ in depth sampled by the micro-electrode. Moreover, the rate was similar from one experimental animal to another and tended to remain at a constant value for long periods of time.

If, however, body temperature changed, this background level altered (Lippold & Redfearn, 1960; Bindman, Lippold & Redfearn, 1963) as it also did when loud noises occurred.

Electrical circuits, etc. In our early experiments we often failed to obtain a prolonged increase in firing following positive polarization of the required duration. We found later that if the current was rapidly cut off, cortical depression could be induced near the electrode tip. It was therefore essential to reduce current strength gradually and to ensure that no unwanted transients occurred in the polarizing circuit.

The site of the indifferent electrode proved to be immaterial.

RESULTS

Immediate effects of polarization of cerebral cortex

On the evoked potential. The normal evoked potential recorded at the surface of the sensory cortex in the rat anaesthetized with urethane, consists of an initial small positive (or often diphasic positive-negative) wave (1) occurring about 5 msec after the stimulus to the forepaw. This is followed by a larger positive wave (2) of latency 7–9 msec, and a negative wave of variable size and shape (3) of latency 10–15 msec and up to 25 msec in duration. Waves (2) and (3) are probably mainly post-synaptic in origin; the positive wave (2) is due to the depolarization, at a depth, of neurones which have processes leading to the cortical surface, and the negative wave (3) occurs when excitation has spread to the surface elements also (Eccles, 1951; Cragg, 1954; Cragg & Hamlyn, 1955; Chang, 1959).

The configuration of the normal variable evoked potential recorded from the cortical surface (Lippold, Redfearn & Winton, 1961) has been shown to be related to the pre-existing potential level of the cortex (Bindman *et al.* 1964).

When the potential level of the cortical surface was altered by the passage of polarizing current, the size and form of the evoked potentials were changed (as shown by Bishop & O'Leary, 1950). A potential applied to the polarizing electrodes such that the surface was positive with respect to deeper structures, resulted in a modification of the evoked potentials, positive wave (2) being reduced in amplitude or abolished and negative wave (3) being increased in amplitude and duration.

Figure 1 shows these changes produced by a current of 0·25 μA/mm^2 pial surface area flowing across the thickness of the grey matter of the somato-sensory cortex, whilst potentials were evoked every 2 sec by stimuli given to the contralateral forepaw. (*a*) shows the effect of surface-negative current

flow, (*b*) is a normal control, and (*c*) is the effect of surface-positive current. It will be noted that the large negative waves of the evoked potentials in (*c*) are not simply a mirror image of the positive waves in (*a*), for their latencies differ.

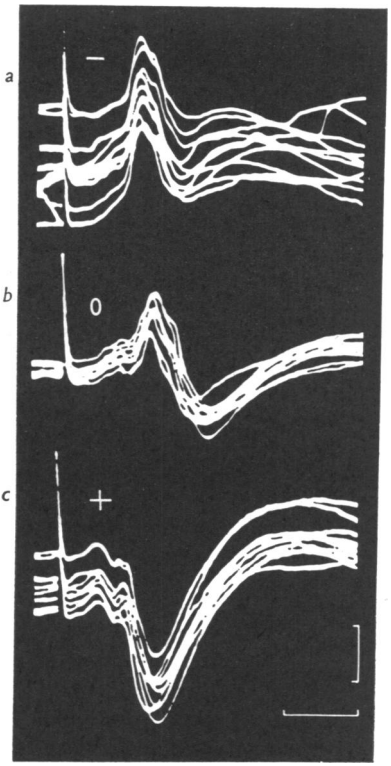

Fig. 1. Traces of ten superimposed consecutive potentials evoked by stimuli at 2 sec intervals to forepaw. Records from surface of contralateral somatosensory area. (*a*) Effect of surface-negative polarization (3 μA total current flow). (*b*) Normal traces showing waves, (1), (2) and (3) (see text, p. 371). (*c*) Effect of surface-positive polarization (3 μA). (Electrode wick in saline cup; surface area of exposed pia = 12 mm^2.) Voltage calibration = 1 mV; Time bar = 10 msec. Each set of ten traces was taken less than 1 min after the preceding set. In this and subsequent figures an upward deflexion of the trace indicates that the recording electrode is positive with respect to the indifferent electrode.

On spontaneous activity. In the anaesthetized cortex, a micro-pipette thrust into the grey matter revealed continuous neuronal activity. Unit discharges could be recorded at any depth deeper than 500 μ in the cortex; the mean firing rate appeared to be constant during long periods of time provided that body temperature and the anaesthetic depth did not vary unduly. A single cell usually discharged in bursts at a frequency of up to 50/sec in the burst and had an inter-burst interval of from 0·3–1·5 sec.

Surface-positive polarization was found to raise the mean firing rate of these neurones and to activate cells which were previously silent while surface-negative polarization either reduced the spontaneous firing or completely inhibited it (Fig. 2).

These results confirm the work of Burns (1957), Calvet & Scherrer (1961, 1962) and Creutzfeldt, Fromm & Kapp (1962). We also found that if polarizing current was passed through the micro-pipette tip instead of from the surface while recording was in progress, a tip-positive current of 0·05–0·25 μA (0·5 μ–1·5 μ internal diameter at tip) would nearly always

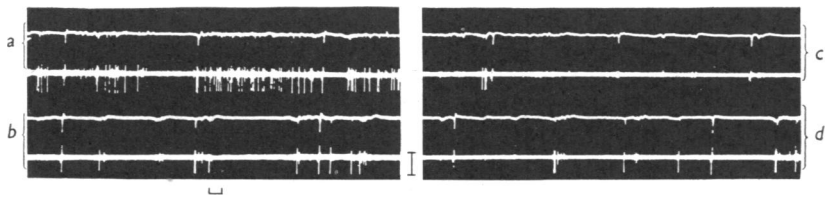

Fig. 2. Effect of radially applied polarizing current of 10 μA on unit discharge. Current density across pia approx. 0·5 μA/mm². (*a*) Positive, (*b*) control, (*c*) negative and (*d*) control periods. Voltage = 1 mV; Time = 200 msec. Top trace of each pair shows evoked potential at approximately every 2 sec. Bottom trace shows unit firing at 880 μ below pia recorded with micro-electrode filled with 11 % KCl.

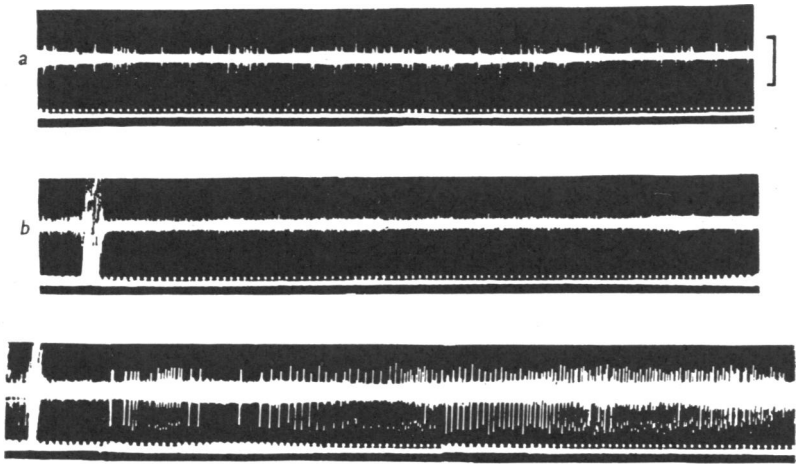

Fig. 3. The effect of polarizing current passed through recording micro-pipette on unit discharge 650 μ below pia. (*a*) control period (*b*) during tip-negative polarization, current flow 0·1 μA and (*c*) during tip-positive polarization, current flow 0·25 μA. Large units in (*c*) of the order of 1 mV. Note increased thickness of base line which was due to the firing of low amplitude units. Large artifacts at beginning of records (*b*) and (*c*) indicate when current was turned on. Time signals, 10 msec intervals; voltage = 1 mV (tip diameter approx. 1·5 μ).

produce an enhancement of unit discharges. Both frequency of discharge of a single unit and the number of active units were increased in this way. Tip-negative current inhibited firing and if the current strength was increased to high enough levels often all activity could be abolished (Fig. 3). In a number of experiments we found the opposite effect, namely that tip-negative current increased firing rate. This point is discussed later (p. 380).

It was noticed that the changes described above (and particularly those involving the evoked potential) usually did not reach a maximum immediately a constant polarizing current was passed. A period of several minutes usually elapsed before the peak of the effect was reached and also the effect often persisted for a time after the current was switched off. Intermittent passage of current and reversal from one polarity to the other enhanced the resultant effect. The remainder of this paper concerns this prolonged after-effect and the conditions necessary to produce it. A preliminary report has already been published (Bindman, Lippold & Redfearn, 1962*b*).

After-effects of polarization of cerebral cortex

On evoked potentials. If the polarizing current was passed for about 5 min or longer, there was a persistent change in peak amplitude of the negative wave when recorded at the depth of minimum latency (300–500 μ below the pia) or recorded as negative wave (3) on the surface. This long-lasting change was in the same direction as that produced by the polarizing

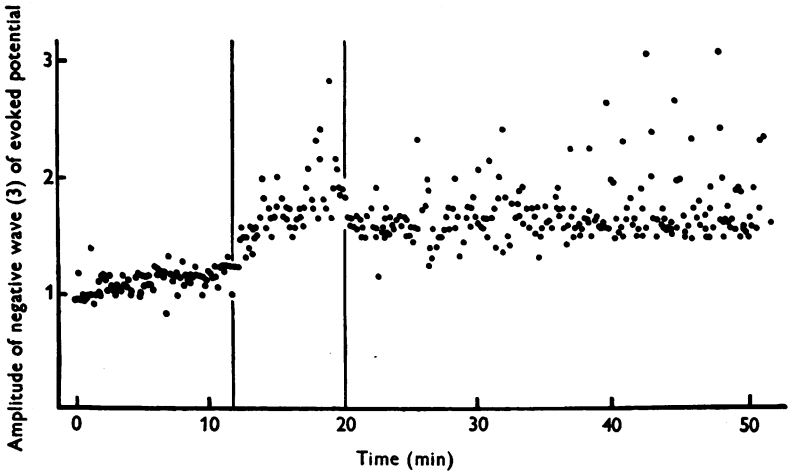

Fig. 4. The after-effect of surface-positive polarization on the peak amplitude (mV) of the evoked potential. (Negative wave (3), recorded from the depth of minimum latency.) Between the 12th and 20th min a current of 25 μA was passed radially through the somatosensory cortex. Area of exposed pia 12 mm^2.

current, i.e. a surface-positive polarization of 5 min would give rise to a prolonged increase in size of evoked potentials. Figure 4 shows the effect of passing 5 μA surface-positive current using a wick electrode resting on the exposed pial surface of the brain immediately over the recording site. The area in contact with the exposed pial surface of the brain was 0·5 mm^2.

There are several factors which appear to be necessary in order to produce this after-effect satisfactorily.

(*a*) It is essential to remove the dura near the point of contact of the polarizing electrode.

(*b*) The polarizing and recording electrodes must be within 1 mm of each other.

(*c*) The temperature of the rat and its cortical surface must be kept constant. A change of 1–2° C would give rise to large changes in size of evoked potentials (see Lippold & Redfearn, 1960).

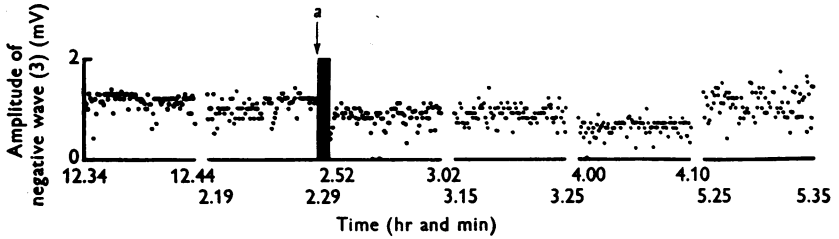

Fig. 5. The effect of surface negative polarization on the amplitude of negative wave of evoked potentials; at *a*, a current of 20 μA was passed between a non-polarizable wick electrode on the surface (negative) and an indifferent electrode buried in a distant muscle. The effect is relatively small in magnitude because it is difficult to adjust current flow to a suitable value which will not produce complete cortical depression and yet will give rise to a long-lasting after-effect.

Figure 5 shows the after-effect of negatively polarizing the cortical surface. This is also an effect lasting for long periods of time but since cortical depression (Leaõ, 1944) resulting from overstimulation, damage, potassium accumulation, etc., is difficult to differentiate from this effect we have, for the present, spent little time in its investigation.

The effect of cortical depression produced by polarizing with too large a current is shown in Fig. 6. At the end of the period of polarization the current was increased from 20 to 200 μA for a couple of seconds. There followed a complete abolition of the evoked potential which, however, gradually recovered during the next $\frac{1}{2}$ hr. It is interesting to note that ultimately the amplitude was increased by this procedure in spite of the period of depression.

In general, there was little correlation between the duration of the prolonged effects we have described or the percentage change in amplitude of evoked potentials and the alterations in size of the evoked potentials that occurred actually during polarization, although if there was no change during current flow very often there was also no after-effect.

On spontaneous cortical activity. If current was passed between a comparatively large surface wick and an indifferent electrode, as described in the previous section, a prolonged after-effect could be obtained on the firing rate of individual cortical neurones in the absence of any specific or other stimulation. However, we hoped that we could get evidence to show whether the long lasting effect was a local one involving only cortical cells, by reducing the volume of cortex which was affected by the polarizing current.

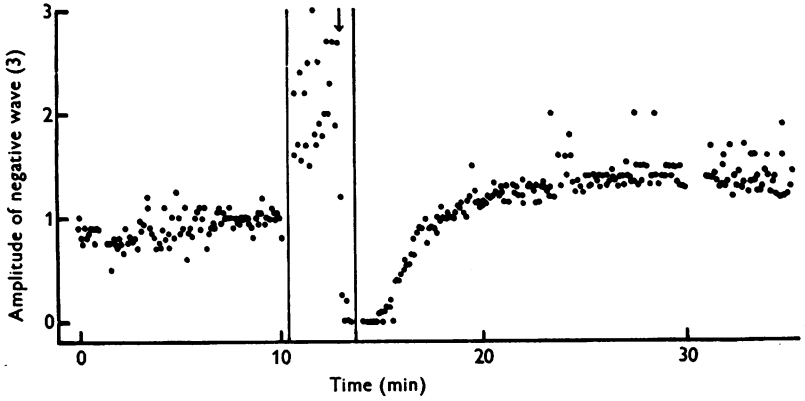

Fig. 6. Cortical depression produced by passage of large surface-positive polarizing current. At 11th min, 20 μA positive polarization was applied; at 13th min (arrow) this was increased to 200 μA for 2 sec. All activity was abolished. The evoked potentials gradually increased in amplitude from zero during the subsequent $\frac{1}{2}$ hr, eventually reaching a higher level than in the initial control period. Ordinate in mV. Experimental procedure as in Fig. 4.

Initially, attempts were made to produce an after-effect by polarizing between two microelectrodes whose tips were 2–5 μ in dia and 50–100 μ apart. This proved difficult to achieve, and several penetrations were required to place the tip of the recording electrode in the vicinity of the tip of the polarizing electrodes. The occasional success, however, did indicate that the polarized zone was sharply demarcated and the increased activity could not be detected for more than about 100 μ in any direction outside the affected region.

The method of local polarization finally adopted was to make use of the recording electrode; currents of the order of 0·1–0·5 μA were passed between its tip (internal dia. 0·5–1·5 μ) and an indifferent electrode. During the initial control period the polarizing circuit was completely disconnected. During the passage of current it was still possible to record the frequency of spike discharges, although there were measurable changes in the amplitude of each spike. These amplitude changes were almost certainly due to the sum of two effects; first, the polarizing circuit represents a shunt across the

input of the amplifier; second, the current flow produces changes in actual spike voltage. At the end of polarization, the polarizing circuit was again disconnected so that recording conditions were strictly comparable with those obtaining beforehand. (It must be emphasized that all our results concern spike frequency. Changes in amplitude, shunting effects, etc., should not affect the conclusions in any way.)

The passage of 0·1–0·25 μA through the micro-electrode for a period longer than about 5 min resulted in a more or less permanent change of firing frequency. In general, when the tip was positive, spontaneous firing increased and there was a prolonged elevation in cortical unitary activity. When the tip was negative, firing was decreased and remained decreased for prolonged periods of time after the polarizing circuit was disconnected. There were occasions when tip-positive current would inhibit firing but this seemed to be the case when only a single unit was being studied, the action potentials were large and initially positive in sign and it was clear that the micro-electrode was very close to the cell soma. We tried to avoid this situation because very often under these circumstances the margin between the current strength required to affect the cell and the current which irreversibly injured it was so small that it was impossible to produce long-term effects. Moreover, small movements of the electrode tip during the period of current flow would alter the current density and so spoil the experiment. Our aim was rather to record from a group of about five cells with an electrode which was not close to any one of the cell bodies. When we did this, polarization with the tip positive resulted in an increase in firing during the current flow, and a prolonged increase afterwards if the duration of current flow was long enough. Presumably this indicated that we were inducing current flow into dendritic cell processes and an outward flow through the soma membrane, thus increasing the excitability of the cell. This may have reflected the fact that the dendrites of a given neurone are spread throughout a zone in the grey matter which is large compared with the volume of the cell body or it may have depended solely upon the relative areas of the dendritic and somatic membranes.

In Fig. 7 is shown the result of polarizing for a period of 20 min with a tip-positive current flow of 0·25 μA with an electrode of diameter 1 μ filled with 10 % NaCl. The firing frequency can be seen to increase during and after the current flow. In some experiments the increase was fourfold but usually it was less than this.

Figure 8 shows photographic records of the action potentials which were being counted during the experiment illustrated in Fig. 7*a*.

We found that subsequent passage of polarizing current often enhanced the effect and it was possible to produce an increase in firing rate of neurones in a series of steps.

If the positive current which was passed through the micro-electrode

tip was too large (0·5–2·0 $\mu A/\mu^2$ in most experiments), a depression of activity was produced. Sometimes, as described previously in the case of experiments on evoked potentials, the count would rise to above the control level after the depression had passed off.

As a rule the enhancement of spontaneous firing was not at its maximum

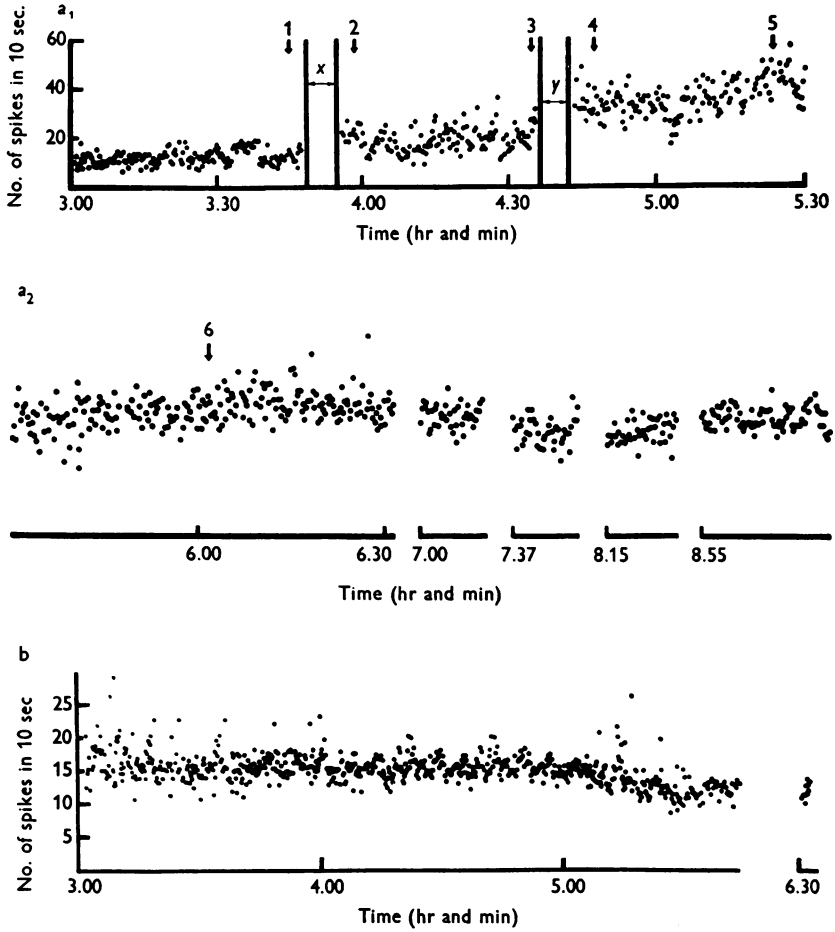

Fig. 7. (*a*) The effect of polarization of grey matter through a micro-pipette. Plotted points are no. of action potentials in 10 sec periods, recorded from the same electrode. At x and y, a current of 0·25 μA with the tip positive was passed for 20 min. At the arrows, oscilloscope records of the action potentials being counted were taken and are shown in Fig. 8. The tip was 500 μ below the pia in the primary somatosensory receiving area for the forepaw. (a_1 and a_2 are a continuous record.) Internal diameter of tip = 1 μ. (*b*) A control record obtained in precisely the same manner but on a different experimental animal, without any polarizing current having been passed. Note that vertical scale on control record is expanded.

immediately after the polarizing circuit was disconnected. Often the firing rate would continue to increase for 15–30 min afterwards (see Fig. 7*a*). Also we often observed a periodicity in the frequency count following the passage of current; there were temporary increases in firing about every 15–20 min each lasting for perhaps 3–5 min.

We are unable at present to determine the length of time for which the effects of polarization last. The experiment shown in Fig. 7*a* is typical and shows the enhancement of spontaneous firing to be essentially undiminished 5 hr after the current was first applied. In other experiments

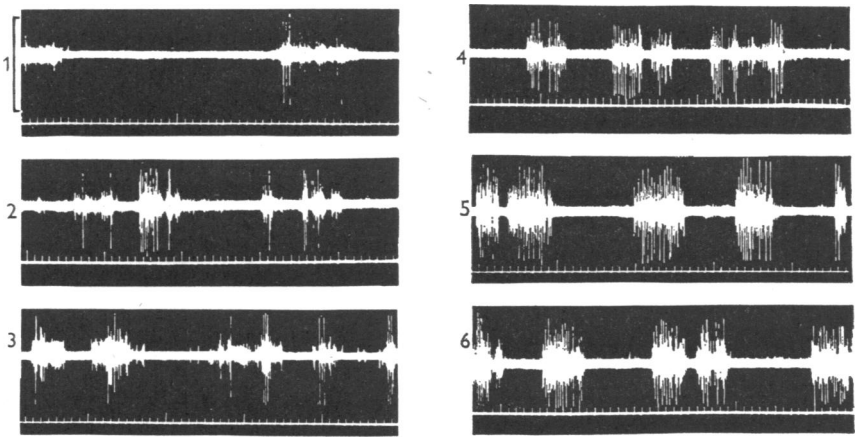

Fig. 8. Records of spike activity taken during the experiment of Fig. 7*a* at the times indicated by the arrows in that figure. Voltage calibration = 0·5 mV. Time = 1 sec.

we observed effects lasting for 1–3 hr and declining with time. It would be necessary to use survival experimental techniques to determine the true time course of the effects we are describing.

In the rat cortex anaesthetized with urethane, unitary activity occurs in a series of 'bursts' or groups of spikes. Positive polarization tended to increase the number of bursts present in a given time interval, to increase the duration of each burst, but not greatly to change the firing pattern within each burst. This pattern of activity is to some extent a function of the type of anaesthetic used and particularly of the depth of anaesthesia. We have postponed a more detailed investigation of this point.

As described previously in the case of the effects of polarization on the evoked activity of the cortex, tip-negative currents produced a decrease in firing which was prolonged after the current was switched off, provided that the duration of flow was longer than about 5–10 min. Figure 9 shows a typical result of this type. For the reasons previously stated we have again not investigated this effect in detail.

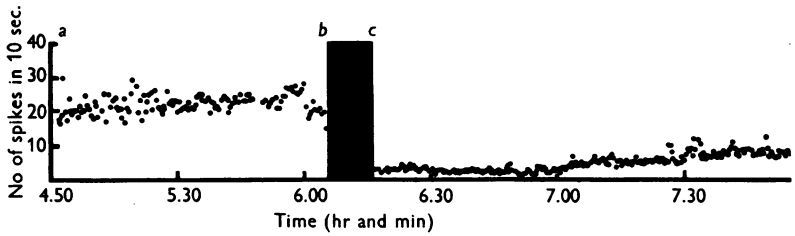

Fig. 9. Effect of tip-negative polarization. Micro-electrode 5 μ diameter, 10% NaCl. *a–b* control period. At *b* 0·3 μA on. Discharge frequency declines until *c* when current circuit disconnected. From *c* the depression of spike activity persists for more than 2 hr. Rat, wt. 220 g, anaesthetized with 0·9 cc 36% urethane at 1·50 p.m. The recording was made from a depth of 500 μ below the pia in the primary sensory receiving area of the forepaw.

The potential fields within the grey matter were roughly measured to determine whether or not they fell within the physiological range. This was done by obtaining values for the standing potential at various points in the vicinity of the polarizing micro-electrode when it was in use. The tip locations of both electrodes were determined by calculation from their polar co-ordinates measured with the micromanipulator scales. It was impossible to make valid measurements when the two tips were closer than about 25 μ. When a current of 0·1 μA was passed through the micro-electrode, the maximum potential gradient that could be recorded near its tip in four experiments was 0·25 mV/100 μ. There are slow potential shifts which occur spontaneously in the anaesthetized rat cortex of up to 2 mV in 0·5 mm (Bindman *et al.* 1964).

DISCUSSION

We have shown that a low-magnitude alteration of the physical environment of certain neurones, lasting for a few minutes, causes a prolonged change in their rate of activity. This is of considerable interest in connexion with the possibility that the mechanisms underlying the phenomenon also play a part in the formation of memory traces, learned behaviour and possibly the process of conditioning.

We found that polarization with the tip of the micro-pipette positive under the conditions of our experiments resulted in an increase in firing rate of cortical cells.

B. D. Burns (personal communication), Krnjević & Phillis (1963), Curtis & Koizumi (1961) and Burns & Salmoiraghi (1960), all working with the cat, found that tip-positive flow always gave inhibition of a neurone from which negative spikes were being recorded. Only when the tip of the electrode recorded large positive action potentials did they find that tip-positive flow had an excitatory effect. In the rat the distances between the cell body and its dendritic tree are smaller than in the cat and the size of the electrode tip relative to the cell diameter is greater. In most of our experiments, therefore, it was likely that the spatial relation between the

positive electrode tip and the cell was such that current flow was inwards through the dendritic processes and outwards via the soma.

At the moment we are not in a position to discuss the way in which polarizing current acts on a neurone to alter its *long-term* excitability.

In none of our experiments were epileptiform after-discharges seen either during the period of current flow or following its disconnexion. Pinsky & Burns (1962) have shown that the establishment of an epileptic focus in the cortex depends on the excitation of a critical, minimum number of neurones. These neurones must, in addition, be stimulated to reach a critical state of exhaustion and it is during the recovery from this phase that the after-discharges occur. We were able, with either polarity of current flow, to initiate cortical depression (Leaõ, 1944) if the current density was high enough, without the appearance of after-discharges at any current strength up to this value. Thus it would appear that the underlying mechanism of the long-term response to polarizing current is different from that producing an epileptic discharge as a result of cortical stimulation.

There is some evidence that the determining factor in producing long-lasting after effects is the change in firing rate of neurones rather than the orientation of the current flow that produces the change. Thus G. K. Smith (personal communication) finds that subcortical stimulation which increases firing frequency in cortical neurones can give rise to a subsequent prolonged elevation in firing rate. We have also found that local cooling, which increases the unitary firing frequency in the rat cortex (Bindman, *et al.* 1963), can result in an increase of mean frequency lasting for at least five hours provided that the period of cooling is maintained for ten minutes or more (Gartside & Lippold; to be published). It is perhaps interesting to note that cooling the surface of the cortex induces a potential gradient in the opposite direction to that required to increase the mean firing frequency of cortical units, when using trans-cortical polarizing currents.

SUMMARY

1. The effects of brief passage of polarizing currents through the cerebral cortex of the rat are described.

2. Surface-positive current enhances neuronal firing and increases the size of evoked potentials; surface-negative current has the opposite effect.

3. If current flow is prolonged for 5–10 min, a persistent after-effect in the same direction is produced, lasting often without decrement, for at least 1–5 hr.

4. Polarization through a glass micro-electrode with currents of about

0·1 μA, confined to cells in the immediate vicinity of the electrode tip, has similar persistent effects to those described above.

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